tion and its high metabolisation in glucuronides (GC), suggesting that these metabolites are susceptible to express HT biologicial activity *in vivo*. Our objective was to compare the vasorelaxant effect of Res, HT and GC on isolated aortic from young males Wistar rats (3months), old Wistar and GK rats (14 months), in presence or not of *t*-BOOH-induced oxidative stress (1mM; 30min). No vasorelaxant effect of the polyphenols was observed in young or old males Wistar rats. However, in old GK rats, Res and GC had significant vasorelaxant effect. In response to *t*-BOOH-induced oxidative stress, HT and RES protected the aortic rings of young Wistar rats ($p < 0.05$). However, different maximal relaxation was found between HT + *t*-BOOH, Res + *t*-BOOH and Control (72.5 ± 2.8%, 76.1% ± 7.7% vs 88.8 ± 0.7% ; $p<0.05$). The sensibility to Ach (EC_{50}) was altered negatively in Res + *t*-BOOH and *t*-BOOH in comparison of Control (2084.6 ± 1687 nM, 2983.5 ± 1110 nM vs 66.9±10.7 nM). The protective effect of HT and RES against the acute effect of *t*-BOOH-induced oxidative stress in a normal context tends to confirm our results in old GK rats, highlighting an effect of these polyphenols only in a pro-oxidant context.

0325

Catabolism of leucine in the heart inhibits glucose transport

Edith Renguet (1), Audrey Ginion (1), Roselle Gélinas (1), Julien Auquier (1), Louis Hue (1), Christine Des Rosiers (2), Jean-Louis Vanoverschelde (1), Sandrine Horman (1), Christophe Beauloye (1), Luc Bertrand (1)
(1) Université Catholique de Louvain, Bruxelles, Belgique – (2) Université de Montréal, Montreal Heart Institute, Montréal, Canada

Branched-chain amino acids like leucine induce insulin resistance in muscle and adipose tissues. The mechanism explaining leucine action involves mTOR/p70S6K signaling. This pathway is activated by leucine and is implicated in the stimulation of an insulin negative feedback loop. Knowing that insulin-resistance participates in diabetic cardiomyopathy, we were interested in studying leucine action in cardiomyocytes. Primary cultured adult rat cardiomyocytes were pretreated with different concentrations of leucine (1 to 10mM) during different periods of time (up to 20h) before being exposed to insulin (3x10-9M, 30min). Insulin increased glucose transport. This correlated with the increase of PKB and AS160 phosphorylation, both known to regulate GLUT4 translocation to the plasma membrane allowing glucose uptake. 1h pre-incubation with leucine stimulated mTOR/p70S6K pathway. This is accompanied by a decrease in PKB and AS160 phosphorylation but, surprisingly, insulin-stimulated glucose uptake was preserved. On the other hand, a longer incubation (14h) with leucine induced a drastic decrease in glucose transport. The mTOR/p70S6K inhibitor rapamycin did not prevent this inhibition. The non-metabolized leucine analog BCH had no effect on the insulin-induced glucose uptake. By contrast, intermediates of leucine catabolism, alpha-ketoisocaproate and ketone bodies inhibited glucose uptake similarly to leucine. This inhibition is clearly independent of insulin signaling because leucine also inhibited basal glucose transport and glucose uptake stimulated by the insulin-unrelated pathway involving AMPK. The leucine-mediated inhibition of glucose transport resulted from the inhibition of GLUT4 translocation. The exact molecular mechanism downstream leucine's metabolites and responsible for the inhibition of GLUT4 translocation and glucose uptake is under investigation. Leucine catabolism reduces cardiac glucose transport independently of insulin signaling by an undefined mechanism.

0136

Effects of piceatannol on cardiac remodelling in obese Zucker rats

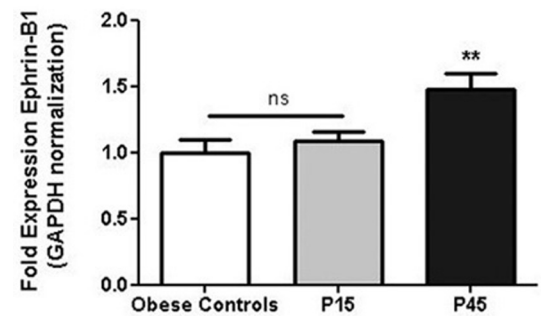
Fanny Leboulanger (1), Céline Guilbeau-Frugier (2), Célie Mias-Vigouroux (3), Marie-Hélène Séguelas (3), Du N'Guyen (3), Céline Galés (3), Jean-Michel Senard (1)
(1) CHU Toulouse, Pharmacologie médicale et clinique, Toulouse, France – (2) CHU Toulouse, Anatomie pathologique, Toulouse, France – (3) CHU Toulouse Rangueil, INSERM UMR 1048, Toulouse, France

Background/Objective: Despite piceatannol is a polyphenol belonging the stilbene family as resveratrol, only very scarce studies have adressed its effects in obesity. Thus, our objective was to analyze the potential effects of piceatannol on cardiac tissue remodelling associated with the development of diabetes and obesity in Zucker rats (fa/fa) rats. This study was part of the POLYFrEsNOL study granted by the REFBIO network.

Methods: Zucker rats aged 6 weeks purchased from Charles River (France) were placed in an air-conditioned room (22C° ± 2°C with a 12 h light – dark cycle. They were fed with a normal diet and received 15 mg/kg (P15, n=10) or 45 mg/kg (P45, n=10) of piceatannol or vehicle (Ctl, n=10) during 42 days. After euthanasia, hearts were removed for histomorphological analysis including measurement of cardiomyocyte size (membranes were stained using WGA) and quantification of fibrosis (trichrome of Masson) as well as measurement of the cardiac expression of ephrin-B1 (western-blot). Data are presented as mean ± SD and were analyzed using one-way ANOVA.

Results: Piceatannol, whatever its dosage, failed to prevent the weight increase induced by HFD (Ctl: 170±32 g, P15: 168±23 g, P45: 169±26 g). No differences in heart weight/body weight ratio (mg/g) was noticed (Ctl: 2.74±0.20, P15: 2.55±0.20, P45: 2.58±0.22, NS). Piceatannol (15 and 45 mg/kg) failed to reduce cardiomyocyte hypertrophy or heart fibrosis deposition. A significant increase in ephrin-B1 expression ($p<0.01$ vs Ctl) in whole heart tissue was noticed in the P45 group but not in the P15 group (Fig 1).

Conclusion: Piceatannol does not prevent cardiac tissue remodeling associated with obesity and diabetes in this model. However, the increase in ephrin-B1 expression suggests that it could have some protective properties against cardiomyocyte lateral membrane remodeling. This finding would justify new studies investigating its effect on lateral membrane structure using electron microscopy.



Abstract 0136-Figure: Ephrin-1 expression in heart in obese rats